PATENT
Attorney Docket No. 0803-0111

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Examiner: Carolyn A. Paden
Dilip K. Nakhasi	
Roger L. Daniels	Group Art Unit: 1781
For:	
STRUCTURED LIPID CONTAINING COMPOSITIONS AND METHODS WITH HEALTH AND NUTRITION PROMOTING CHARACTERISTICS	Confirmation No. 1274
Filed: March 8, 2004	
Serial No.: 10/795,843	

DECLARATION OF DILIP K. NAKHASI UNDER RULE 132

I, Dilip K. Nakhasi, do hereby declare as follows:

1. I am one of the named inventors of the above-captioned patent application and am employed as Team Director, R&D Innovations of the proprietor of this application.

2. I hold the following academic degrees: Bachelor of Science degree in Agricultural Sciences (with Honors) from University of Meerut, Meerut, India, awarded in 1984; and a Bachelor of Science degree in Food Science & Technology from University of Maryland, College Park, Maryland awarded in 1989.

3. I have been employed as a scientist in the food industry with substantial food science experience for at least 22 years. Throughout this time I have had extensive experience in the technology of edible oils as well as other facets of organic chemistry, including working knowledge of the synthesis and formulation of edible oils as well as functions and effects of oil compositions on health and nutrition promotion.

4. I have been informed that claims of the above-captioned application have been rejected as being unpatentable from Aoyama U.S. Patent No. 6,827,963 of The Nisshin OilliO, Ltd. ("Aoyama") as the primary reference, together with various other references.

5. I have considered the Office Action dated July 22, 2011 and particularly the statements in support of the rejection regarding enhancing phytosterol delivery and regarding a clinical study reported in a 2006 publication of which I am a co-author.

6. Example 15 of the subject application provides a showing that random interesterification is a means of enhancing phytosterol delivery. Test data are reported at paragraphs [0098] through [0102] of the published version of the subject application, namely Patent Application

Publication No. 2005/0196512. This Example 15 reports that phytosterol-containing edible oil compositions were incorporated into five food products. In each case, two types of edible oil compositions were considered. One type was a lipid interesterified from caprylic and capric medium-chain triglycerides and canola oil as the long-chain domestic oil "inventive oil". This oil was modified to include 6 weight percent phytosterol ester as an inventive oil composition. The other type was the "control oil" composition, which was canola oil containing 6 weight percent phytosterol ester. Canola oil is generally recognized as beneficial to human health, being low in saturated fat, cholesterol-free, sodium-free, high in monounsaturated fat, and contains beneficial omega-3 fatty acids.

7. In the testing outlined in paragraph 6 above, both the control oil and the inventive oil compositions were separately used to stir fry different groups of the same vegetables. While only 90 mg of phytosterol were found in the vegetables cooked in the control oil composition, 410 mg of phytosterol were found within the same weight of vegetables cooked in the inventive oil

composition, representing a **phytosterol delivery enhancement of over 4.5 times.**

8. Separate quantities of the same weight of chicken were pan fried in the control oil composition or the inventive oil composition. The control oil chicken had 30 mg of phytosterol, while the inventive oil chicken had 200 mg of phytosterol. This is a **phytosterol delivery enhancement of 6.6 times.**

9. Separate quantities of the same weight of muffins were baked in the control oil composition or the inventive oil composition. The control oil muffins had 30 mg of phytosterol, while the inventive oil muffins had 160 mg of phytosterol. This is a **phytosterol delivery enhancement of 5.3 times.**

10. Separate quantities of the same weight of yellow cake batter were baked in the control oil composition or the inventive oil composition. The control oil cake batter had 50 mg of phytosterol, while the inventive oil cake batter had 300 mg of phytosterol. This is a **six-fold phytosterol delivery enhancement.**

11. Separate quantities of the same weight of waffle batter were baked in the control oil composition or the inventive oil composition. The control oil cake batter had

10 mg of phytosterol, while the inventive oil cake batter had 70 mg of phytosterol. This is a **phytosterol delivery enhancement of seven-fold.**

12. The test data recited above illustrate the feature of the present invention of enhanced phytosterol delivery. The magnitude of the enhancements shown by these data is a significant difference, and same is due to the use of the random interesterified oil composition as the delivery vehicle for the phytosterol.

13. The clinical study identified in paragraph 5 of this Declaration, which was completed after the filing of the present application, is reported in the publication "Phytosterols mixed with medium-chain triglycerides and high-oleic canola oil decrease plasma lipids in overweight men," Rudkowska et al., *Metabolism Clinical and Experimental*, 55, pages 391-395 (2006). I am a co-author of this publication, already of record in the present application. The entirety of this publication is respectfully incorporated by reference hereinto, by virtue of which the facts of this publication are placed into the record of this application in Declaration form.

14. The 2006 Rudkowska publication reports the results of clinical testing with the inventive oil

composition of random interesterified caprylic, capric and oleic oils and phytosterol versus a control oil of extra virgin olive oil. Extra virgin olive oil is recognized as an especially valuable lipid for cholesterol reduction and is considered to be one of the "gold standard" oils for improving circulatory lipid patterns. In contrast, the interesterified oil of the inventive oil composition is in the category of "synthetic" oils that often are prejudged as unhealthy.

15. One of the references relied upon in the Office Action concerns blends of medium-chain triglyceride oil and phytosterols, without any suggestion that the MCT oil is to be interesterified with a long-chain domestic oil. This cited reference is "Consumption of a Functional Oil Rich in Phytosterols and Medium-Chain Triglyceride Oil Improves Plasma Profiles in Men," St.-Onge et al., *Human Nutrition and Metabolism*, pp. 1815-1820 (2003). Such a blend of 2003 St.-Onge is not an interesterification, as is the case for the inventive oil composition of Rudkowska.

16. The 2006 Rudkowska publication and the 2003 St.-Onge publication each report on clinical testing of men having a body mass index of 25-31 kg/m^2. Twenty-three of these men completed the study using applicants' invention,

while thirty men were in the study of the 2003 St.-Onge publication. Each study followed a randomized crossover type of test, and each delivered the phytosterol-containing component with the same isoenergetic meal protocol of 15% protein, 40% fat and 45% carbohydrates. In the 2006 Rudkowska publication clinical study using applicants' inventive oil composition, blood samples were taken at days 1, 2, 41 and 42, whereas in the 2003 St.-Onge clinical study, blood samples were taken at days 1, 28 and 29. Each analyzed the blood samples and calculated LDL cholesterol using the Friedenwald formula.

17. The Baseline LDL for applicants' inventive oil composition, as reported in Rudkowska, was 3.95, same being reduced to the End point value of 3.12, **a reduction of 21%.** *See* data in the table on page 393 of Rudkowska in the "Functional Oil" columns and the "LDL-C" rows.

18. The Baseline in Rudkowska for the extra virgin olive oil was 4.00, same being reduced to an End point of 3.54, **a reduction of 11.5%.**

19. As reported in Table 3 on page 1817 of the St.-Onge publication, the Baseline for the functional oil (FctO) for LDL-C was 3.43, and the Endpoint was 2.96, **a reduction of 14%.**

20. Thus, according to the respective clinical study data of paragraphs 17 and 19 of this Declaration, the inventive oil composition in Rudkowska achieved an increase of 7 percentage points in LDL cholesterol reduction when compared with the St.-Onge clinical study. This represents an enhancement in **LDL cholesterol reduction that is half again the enhancement** achieved by the St.-Onge composition.

21. According to paragraphs 17 and 18 of this Declaration, LDL cholesterol reduction of the inventive oil composition was enhanced by 9.5 percentage points when compared with the "gold standard" extra virgin olive oil, a reduction that is **over 80% again the enhancement** of the olive oil.

22. The respective clinical studies of Rudkowska and of St.-Onge are properly compared due to close similarities in testing protocol. For example, in the top of the first column of page 2 of St.-Onge, the subjects of the study were identified as having a TC (total cholesterol) concentration below 7.0 mmol/L and a TG (triglycerides) of below 3.0 mmol/L, also stating that the subjects had no history of "diabetes, hypothyroidism, hypertension or other known metabolic disorders and had a body mass index between 25 and 31 kg/M^2." I observe from the clinical study noted

in Rudkowska that the average TC of the subjects of the clinical study on the inventive oil composition was 5.90 mmol/L (which is below 7.0 mmol/L), while the TG average was 1.92 mmol/L (which is below 3.0 mmol/L). This is consistent with page 392 of Rudkowska itself, disclosing an LDL-C of more than 3 mmol/L. That same paragraph of Rudkowska states that the subjects were excluded if they had "diabetes, hypertension, hypothyroidism or other known metabolic disorders."

23. These strong similarities between the St.-Onge and the Rudkowska respective clinical studies and the LDL reduction enhancement of Rudkowska versus St.-Onge allow me to state that their respective results were markedly different and exhibit a significant scientific advance due to the use of the random interesterified oil composition. When compared with the Rudkowska extra virgin olive oil results, the random interesterified oil composition achieved an even greater advancement.

24. Statistical analysis of the data in Rudkowska generally utilized the mean ± standard error of the mean. The total cholesterol (TC) values decreased significantly ($p<0.0001$) from baseline to endpoint for the inventive oil composition, 5.68 ± 0.21 to 4.71 ± 0.16 m/Mol/L. A similar

trend was seen with extra virgin olive oil but to a lesser extent ($p=0.0001$), from 5.73 ± 0.18 at baseline to 5.14 ± 0.19 m/Mol/L at endpoint. The endpoint TC after consumption of the inventive oil composition was statistically lower than that of extra virgin olive oil ($p=0.0006$), while the baseline TC data was not statistically different between the inventive oil composition and the olive oil ($p=0.7075$).

25. The LDL cholesterol decreased significantly with consumption of the inventive oil composition from baseline (3.95 ± 0.19) to endpoint (3.12 ± 0.16 m/Mol/L ($p<0.0001$)). The extra virgin olive oil also showed a significant decrease in LDL from 4.00 ± 0.18 to 3.54 ± 0.18 m/Mo/L ($p=0.0002$). The respective endpoints were statistically different ($p=0.0002$). The **inventive oil composition expressed a significantly greater decrease in LDL** compared to extra virgin olive oil, even though their respective baseline values were similar ($p=0.69$).

26. Based on this statistical analysis found in Rudkowska, it can be extrapolated that the LDL reduction enhancement of Rudkowska versus St.-Onge also are statistically significant.

27. The enhancements and differences reported upon in this Declaration exhibit unexpected results in both phytosterol delivery and cholesterol reduction enhancements and illustrate a difference in kind when compared with the references used in rejecting the claims of this application, rather than one of mere degree. The facts presented in this Declaration illustrate a significant, practical advantage in that consumption of the inventive oil composition reduces LDL cholesterol to an extent greater than expected from the prior art.

28. I hereby declare that all statements made herein and of my knowledge are true and that all statements made on information and belief are believed to be true; and I further declare that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued therefrom.

Dated: October 3rd, 2011

Dilip K. Nakhasi